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EXAMINER	
VU, JAKE MINH	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,634	SELA, YORAM	
	Examiner	Art Unit	
	JAKE M. VU	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-48* is/are pending in the application.

4a) Of the above claim(s) *44 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-43 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/18/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicant's Amendment, Declarations, and Information Disclosure Statement filed on 08/18/2010.

- Claims 29-41, 43-45 have been amended.
- Claims 46-48 have been added.
- Claims 29-48 are pending in the instant application.
- Claims 44 and 45 have been previously withdrawn from consideration.

Declaration under 37 CFR 1.132

The Declaration under 37 CFR 1.132 filed 08/18/2010 is insufficient to overcome the rejection of claims 29-43 based upon HEILGENSTEIN (EP 0919236) as set forth in the last Office action because of the reasons provided below in the *Response to Argument* section.

Election/Restrictions

Newly submitted claims 44 and 45 directed to an invention that lacks unity with the invention originally claimed for the following reasons: the original presented claims pertain to composition claims only, whereas claims 44 and 45 pertain to method claims.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 44 and 45 are withdrawn from

consideration as being directed to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicant argues that the present application is a national stage application of an international application and is thus subject to unity of invention rules and not U.S. restriction practice. Unity of invention practice is discussed at MPEP 1893.03(d).

The Examiner finds this argument unpersuasive, because election by original presentation applies to both Unity of Invention practice and U.S. restriction practice. (See MPEP 1893.03(d) formed paragraph *18.21 National Stage Election by Original Presentation in 35 U.S.C. 371 Application*.)

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 41 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, pertaining to "cellulose derivative", **is withdrawn** in view of Applicant's Amendment.

However, upon further consideration of Applicant's Amendment, a new ground(s) of rejection is made as discussed below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 47 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is rejected because they do not identify the structure, material, or acts set forth in the specification that would be capable of carrying out the functional properties recited in the claims, such as “equivalent to the dissolution characteristics to EFFEXOR XR". It appears from the specification that these claimed functional properties are achieved from specific formulations that contain specific ingredients, such as polyvinylpyrrolidone, ethylcellulose and dibutyl sebacate (see Examples). This is also evident by Applicant's arguments filed on 08/18/2010 that the prior art HEILIGENSTEIN having all the ingredients, such as hydrophilic polymer, hydrophobic polymer and plasticizer, but failed to meet the equivalent of EFFEXOR XR. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181,26 USPQ2d 1057 (Fed. Cir. 1993). Accordingly, the ingredients, which makes up the formulation must be clearly and positively specified in order to place one of skill in the art in possession of the claimed

tablets with the desired properties. It is precisely these ingredients that determines the desired properties and without which, one could not replicate the invention.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30, 32, 35, 38, 41 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **are withdrawn** in view of Applicant's Amendment.

However, upon further consideration of Applicant's Amendment, a new ground(s) of rejection is made as discussed below.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 recites "equivalent to the dissolution characteristics of EFFEXOR XR"; however, no dissolution profile of EFFEXOR XR was provided in the specification.

Thus, one skilled in the art would not know the metes and bounds of "the dissolution profile of EFFEXOR XR".

Claim 47 contains the trade name EFFEXOR XR. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trade name is used to identify a particular venlafaxine extended-release formulation and, accordingly, this identification is indefinite.

Note, the Examiner advises limiting the claim to the actual "dissolution profile", rather than the EFFEXOR XR trade name.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over HEILGENSTEIN (EP 0919236) **are maintained** for reasons of record in the previous office action filed on 05/15/2008, 02/03/2009, 02/19/2010 and as discussed below in the "Response to Argument" section.

Upon further consideration of Applicant's Amendment, a new ground(s) of rejection is made as discussed below.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29-43, 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over OSHLACK et al (US 5,472,712) in view of SHERMAN (EP 0797991) and PALOMA COLL (US 5,232,706) as evidence by FDA (Guidance for Industry. *Bioavailability and bioequivalence studies for orally administered drug products - General considerations* (2002)).

Applicant's claims are directed to an extended-released drug composition comprising of: a drug, such as venlafaxine hydrochloride, coated on a nonpareil inert sugar core; a binder, such as hydroxypropyl methylcellulose; a hydrophilic polymeric layer coating functioning as a separation layer, such as polyvinyl pyrrolidone or

hydroxypropyl methylcellulose; a hydrophobic polymer, such as ethylcellulose; a plasticizer, such as dibutyl sebacate.

OSHLACK teaches an extended-released drug composition comprised of: a psychotropic drug (see col. 14, line 29), coated on nu pariel 18/20 beads (see col. 9, line 31-49; and col. 3, line 2-7), which reads on nonpareil inert sugar core; a binder, such as hydroxypropyl methylcellulose (see col. 9, line 50-55); a barrier layer (see col. 9, line 58-64), which reads on a hydrophilic polymeric layer coating functioning as a separation layer, such as hydroxypropyl methylcellulose or any film-former known in the art may be used (see col. 9, line 58-64); a hydrophobic polymer, such as ethylcellulose (see Title; col. 7, line 60-65; and col. 10, line 3) for controlling the drug release rate (see col. 2, line 13-17); a plasticizer, such as dibutyl sebacate (see col. 7, line 53 – col. 8, line 43, especially at col. 8, line 37-38). Additional disclosure includes: plasticizer will further improve the physical properties of the hydrophobic polymer film; rate-modifying agents, such as hydroxypropyl methylcellulose (see col. 11, line 53-65); therapeutic effect for about 24 hours (see col. 4, line 60-61); controlled release profile of the invention can be altered by varying the amount of ingredients or thickness of coating (see col. 9, line 23-30; and col. 10, line 59-61); provides stabilized dissolution of the active agent for FDA approval (see Abstract; and col. 3, line 25-34; col. 5, line 25-30) .

OSHLACK does not teach using a drug, such as venlafaxine hydrochloride; or a separation layer, such as polyvinyl pyrrolidone.

SHERMAN teaches a 24 hour-extended release composition comprised of: a psychotropic drug, such as venlafaxine hydrochloride (see abstract), wherein a film-

coating of ethylcellulose (see pg. 3, line 26) similar to OSHLACK is used to retard dissolution for extended release (see pg. 2, line 19) of the drug to reduce level of nausea and incidence of emesis that attend the administration of multiple daily dosing (see pg. 2, line 55-56).

PALOMO COLL teaches that separation layers made from hydroxypropyl methylcellulose and polyvinyl pyrrolidone are well known in the art (see co. 3, line 4-12).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate venlafaxine a drug, such as venlafaxine hydrochloride into OSHLACK's composition. The person of ordinary skill in the art would have been motivated to make those modifications, because it would improve the stability of the venlafaxine composition and still have 24-hour extended release of the drug to reduce level of nausea. The person of ordinary skill in the art reasonably would have expected success because OSHLACK and SHERMAN both dealt in the same field of endeavor, such as 24-hour extended-release formulations, and used the same film coating of ethylcellulose to control the dissolution rate of the drug.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to incorporate a separation layer, such as polyvinyl pyrrolidone, into OSHLACK's composition. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success, because polyvinyl pyrrolidone and hydroxypropyl methylcellulose are functional equivalents used as separation layers in drug formulation, and OSHLACK teaches any film-form known in the art maybe used.

The references do not specifically teach adding the ingredients in the amounts claimed by Applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results, such as drug release rate to meet the requirement of the Food and Drug Administration approval for generic drug to be bioequivalent by dissolution studies to the reference drug, which is EFFEXOR XR in this case (if needed see FDA at pg. 1-2, 5-6 and 10-11). Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of Applicant's invention.

Note, one of ordinary skill in the art is well versed in FDA regulation for generic drug approval.

Response to Arguments

Applicant argues that it is noted that a nearly identical rejection over the same prior art was made by the present examiner in the Official Action of August 24, 2005, during the earlier prosecution of this case. In applicants' amendment of January 24, 2006, applicants explained to the examiner that the coating of Heiligenstein was an enteric coating while the presently claimed coating was a controlled-release coating

and, therefore, even making the substitutions noted by the examiner, one would end up with an enteric formulation of venlafaxine and not a controlled-release formulation. For these reasons, it was argued that the claimed controlled release formulation could not have been obvious. In the Official Action of April 14, 2006, the examiner stated:

Applicant's arguments, filed on 01/24/06, with respect to the 35 USC §I03 rejection have been fully considered and are persuasive. The 35 USC §I03 rejection has been withdrawn.

The examiner, in reinstituting this rejection, has not explained why applicant's arguments that had previously been considered to be persuasive are no longer considered to be persuasive.

The Examiner finds this argument unpersuasive, because as stated in the previous office action, upon further consideration the rejection is revived because the Examiner noted that the limitations of "extended-release" is in the preamble. The recitation “extended-release” has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In this instance, the intended use is extended-release.

Applicant's argue that the Declarations of Dr. Michael Grimshaw and Dr. Yoram Sela states Heiligenstein's fomulation is referred to as an "enteric formulation" and is pH-dependent, wherein the formulation of the instant invention is an "extended-release" formulation and is not pH-dependent.

In response to applicant's arguments, the recitations "pH-independent" and "extended release" have not been given patentable weight because the recitations occur in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In this instance, Applicant's claims are more broadly recited as the genus of "hydrophilic polymeric" and "hydrophobic polymer" and "binder", wherein the prior art HEILIGENSTEIN teaches using species that are in these the genus of "hydrophilic polymeric" and "hydrophobic polymer" and "binder".

Applicant argues that Dr. Grimshaw notes that paragraph [0010] of Heiligenstein indicates that the active ingredient of the enteric layer is HPMCAS. Dr. Grimshaw explains that those of ordinary skill in the art of drug formulation are well aware that HPMCAS is a completely distinct chemical from hydroxypropylmethylcellulose.

The Examiner finds this argument unpersuasive, because HPMCAS reads on "hydrophobic polymer", such as "cellulose acetate" (see claim 29 and 41). Note,

HEILIGENSTEIN also teaches using hydroxypropylmethylcellulose (see [0010], Example).

Applicant argues that with regard to the examiner's optimization arguments, Dr. Grimshaw notes, in the paragraph bridging pages 5 and 6 of his declaration that a person of ordinary skill in the art seeking to substitute venlafaxine for duloxetine in the enteric formulation of Heiligenstein would optimize for optimal enteric characteristics as this is what Heiligenstein seeks. Completely changing the ingredients and the amounts so as to obtain a pH-independent formulation with extended release would not be optimization of anything taught by Heiligenstein with respect to enteric-coated formulations.

The Examiner finds this the argument unpersuasive, because HEILIGENSTEIN does not need to have the same motivation as Applicant. In this instance, HEILIGENSTEIN motivation to optimize is to adjust the drug release over time, such as where how far along in the small intestine the drug is released. A thicker layer would release the drug later in the small intestine.

Applicant argues that another claimed feature which is not made obvious by Heiligenstein is the statement in the last paragraph of claim 29 that the controlled release layer permits controlled release of the venlafaxine hydrochloride over an approximately 24 hour period. See the first sentence of paragraph [0009] and the last sentence of [0010] of the attached amended specification. Claim 31 does not use the 24 hour parameter but requires that the hydrophobic polymer layer enable controlled release of the venlafaxine hydrochloride over an extended time period. This is not the

case with Heiligenstein, regardless of whether venlafaxine hydrochloride is substituted for duloxetine.

The Examiner finds this argument unpersuasive, because HEILIGENSTEIN teaches that the venlafaxine composition could be given once a day (see pg. 4, line 48), which would be approximately 24 hours. Note, extended time period could be interpreted as 10 second to 1 year, wherein HEILIGENSTEIN's enteric layer could easily extend the time due to the time needed for the enteric layer to break down.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Telephonic Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAKE M. VU whose telephone number is (571)272-8148. The examiner can normally be reached on Mon-Tue and Thu-Fri 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618